REMARKS

I. Introductory Comments

In the Office Action under reply, the claims were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Bäckström *et al.* (U.S. Patent No. 5,952,008) (claims 1-5, 12-15, 17, 18 and 20-25) and under 35 U.S.C. §103(a) as allegedly being unpatentable over Bäckström *et al.* (U.S. Patent No. 5,952,008) in view of Kamei *et al.* (U.S. Patent No. 5,575,987) (claims 6-11, 16 and 19). The rejections are addressed as indicated below.

Claims 1-25 are pending in the application. Claims 1 and 20 have been amended. No claims have been deleted. Consequently, claims 1-25 remain pending.

Support for the amendments to the claims is identified below. Additional support other than that identified below may exist in the specification for one or more amendments to the claims.

Claims 1 and 20 have been amended to recite that the claimed formulation (claim 1) and recited powder (claim 17) are each "substantially free of penetration enhancers." Support for the amendment is found on page 9, line 7.

As support for the claimed subject matter is found in the application as filed, no new matter is introduced by the entry of the above-identified changes to the claims. The changes to the claims are made for clarification purposes only should not be interpreted as acquiescence in any claim rejection.

II. The Rejection Under 35 U.S.C. §102(e)

The Examiner has rejected claims 1-5, 12-15, 17, 18 and 20-25 under 35 U.S.C. §102(e) as allegedly being anticipated by Bäckström *et al.* (U.S. Patent No. 5,952,008). The Examiner has taken the position that Bäckström *et al.* discloses each of the elements recited in claims 1-5, 12-15, 17, 18 and 20-25.

The standard for anticipation is rigorous requiring that every element of the claimed invention be disclosed by a single prior art reference. *See Minnesota Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1565 (Fed.Cir.1992); *Scripps*, 927 F.2d at 1576-77; *Lindemann Maschinenfabrik GMBH, v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed.Cir.1984).

Claims 1 and 20, the two pending independent claims, recite a formulation (claim 1) and a powder (claim 17) that are each "substantially free of any penetration enhancers." In contrast and as pointed out by the Examiner on page 2 of the Office Action, Bäckström *et al.* discloses compositions that include "a mixture of active compounds (A) a pharmaceutically active polypeptide, and (B) an enhancer compound which enhances the systemic absorption of the polypeptide in the lower respiratory tract of a patient." See, for example, Bäckström *et al.* at the following passages: column 1, lines 52-56; column 7, lines 6-8; column 7, lines 11-12; column 7, lines 54-57; column 11, lines 20-22; and column 11, lines 45-46. Moreover, Bäckström *et al.* states that the "use of an absorption enhancer is of critical importance, as the polypeptide alone is poorly absorbed through the lung." See column 4, lines 36-38.

As amended, the claims encompass formulations and powders that are "substantially free of penetration enhancers." Because Bäckström *et al.* does not teach compositions that are substantially free of penetration enhancers, the anticipation rejection cannot stand. Reconsideration and removal of the rejection under 35 U.S.C. 102(b) is respectfully requested.

III. The Rejection Under 35 U.S.C. §103(a)

The Examiner has rejected claims 6-11, 16 and 19 under 35 U.S.C. §103(a) as being allegedly unpatentable over Bäckström *et al.* (U.S. Patent No. 5,952,008) in view of Kamei *et al.* (U.S. Patent No. 5,575,987).

In the rejection, the Examiner recognized certain deficiencies with respect to Bäckström *et al.* Specifically, the Examiner pointed out that Bäckström *et al.* lacks specific disclosure for including certain components such as amino acids, buffer and HAS into the pharmaceutical formulations or powders. In order to address the deficiency of Bäckström *et al.*, the Examiner cites Kamei *et al.* for its teaching of methods for preparing sustained-release microcapsules containing a biologically active substance. After pointing out additional aspects of Kamei *et al.*'s method, (e.g., dissolving the active agent in water and then in an amino acid-containing solution, adding an antiaggregation agent such as mannitol, lactose, glucose, amino acids, and so forth), the Examiner concludes, among other things, that "[i]t would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the preparations of Bäckström *et al.* by adding the specific additives ... because of the disclosed benefits of ... additives in

preparations containing biological actives." See the paragraph bridging pages 4 and 5 of the Office Action.

This rejection is respectfully traversed in view of the following remarks.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the references teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Without regard to the other requirements, it is clear that the Examiner cannot satisfy the second requirement of showing a reasonable expectation of success should the cited references be combined. Thus, even if it could be shown that a suggestion exists to combine the teachings and that all of the claim limitations are taught by the combined teachings of the references, the rejection must nevertheless be withdrawn as there is clearly no expectation of success.

Applicants point out that not only does Bäckström *et al.* describe compositions that include both a pharmaceutically active peptide *and* an enhancer compound which enhances the systemic absorption of the polypeptide in the lower respiratory tract of a patient, but Bäckström *et al.* also **specifically states that use of the enhancer compound is of critical importance since the polypeptide alone is poorly absorbed through the lung.** See Bäckström *et al.* at column 4, lines 36-38. In contrast, the independent claims (i.e., claims 1 and 20) recite, *inter alia*, compositions "substantially free of penetration enhancers." As pointed out in Applicants' specification, "[t]he dry powder compositions of the present invention are readily absorbed through the lung without the need to employ penetration enhancers." See page 9, line 14-15, of Applicants' specification. Thus, based on Bäckström *et al.*, there can be no reasonable expectation of success that formulations or powders lacking "an enhancer compound which enhances the systemic absorption of the polypeptide in the lower respiratory tract of a patient" could be used to deliver a polypeptide to the lungs for subsequent absorption therefrom.

In addition, Kamei *et al.* lacks any disclosure with respect to pulmonary delivery, much less any discussion of the ability of polypeptides to be absorbed through the lower respiratory

tract. Moreover, Kamei *et al.* describes including agents such as "Tween 80" (column 10, line 16) in pharmaceutical preparations for oral administration. Applicants specifically identified Tweens as exemplary penetration enhancers in line 11 on page 9 of their specification. The use of such penetrations is stated by Applicants to be "undesirable" in their preparations. See Applicants' specification at page 9, lines 10-14.

Based on the combined teachings of the cited references, there would be no reasonable expectation of success that formulations or powders that are "substantially free of penetration enhancers" could be used to deliver a polypeptide to the lungs for subsequent absorption therefrom since (a) Bäckström *et al.* stresses the criticality of using such penetrations enhancers, and (b) Kamei *et al.* provides no evidence that contradicts Bäckström *et al.*'s teaching and, in fact, teaches using the very penetrations enhancers Applicants disclose as "undesirable." Consequently, the combined teachings of the cited references do not provide a reasonable expectation of success that powders and formulations lacking such penetration enhancers would provide pulmonary and systemic absorption of a polypeptide. The Examiner's attention is respectfully directed to claims 1 and 20 that clearly recite formulations and powders that, *inter alia*, "substantially lack any penetration enhancers."

Thus, as the requisite reasonable expectation of success is not present, the Examiner has failed to establish a *prima facie* case of obviousness. Although the present discussion focused on the independent claims, the lack of having established a *prima facie* case of obviousness is applicable to all the rejected dependent claims, i.e., claims 6-11, 16 and 19, (as well as all the other nonrejected dependent claims, for that matter). That is, when an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Applicants reserve the right, however, to argue the nonobviousness of each and every rejected dependent claim. Consequently, the argument that the rejected dependent claims "survive or fall" with the arguments provided above is for expediency purposes only and should not be construed as an acquiescence or admission that the subject matter of one or more dependent claims is obvious in view of an independent claim alleged to be obvious.

IV. The Information Disclosure Statement

Applicants have enclosed an Information Disclosure Statement listing those references previously made of record in this family and/or cited in the specification. For the Examiner's convenience, a copy of any reference not included with the enclosed with the Information Disclosure Statement can be obtained in the file corresponding to U.S. Patent Application Serial N0. 10/355,578. Applicants believe that the pending claims patentably distinguish over the references (individually and in combination) listed in the enclosed Information Disclosure Statement. Applicants would greatly appreciate an initialed copy of the forms indicating that the Examiner considered each of the listed references.

V. Conclusion

In view of the foregoing, Applicants submit that the pending claims satisfy the requirements of patentability and are therefore in condition for allowance. Reconsideration and withdrawal of all rejections is respectfully requested and a prompt mailing of a Notice of Allowance is earnestly solicited.

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 620-5506.

Respectfully submitted,
Nektar Therapeutics

Date: May 6, 2003

By: Mark A. Wilson
Mark A. Wilson
Registration No. 43,275

Nektar Therapeutics
150 Industrial Road
San Carlos, CA 94070
(650) 631-3100 (Telephone)
(650) 631-3125 (Facsimile)